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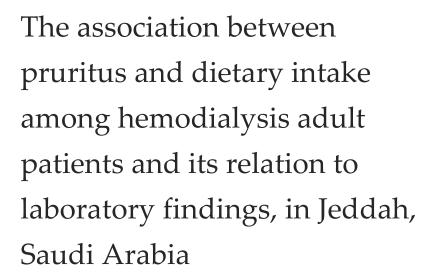
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ABSTRACT

Introduction: Pruritus is a common and bothersome symptom in chronic kidney disease patients, particularly those on dialysis. We aimed to establish the prevalence of pruritus among renal dialysis patients in King Abdulaziz University Hospital and assess its relationship with dietary consumption and laboratory findings. There has yet to be any similar research conducted in this area. Methodology: This was a cross-sectional study started from January to November 2022 during dialysis, 44 patients were interviewed and analyzed in a dialysis clinic. Any patient under the age of 18 was excluded. Pearson's chisquare test, Fisher's exact test and t-test were used to determine the connection between the variables. Results: Pruritus was present in 40.9% of the participants, with an average scale of 4.9/10. The biochemical indicators of kidney function were analyzed quantitatively, in which 100% of the participant had a high pre-dialysis and 11.4% had a high post-dialysis urea. In addition, 36.4% had high phosphorus levels, 29.5% had elevated potassium levels, 6.8% had high albumin and 84.1% had appropriate KT/v. There was a strong association between pruritus and pre-creatinine. The mean precreatinine in the presence of pruritus was significantly different from the mean pre-creatinine in the absence of pruritus (P = 0.005). Conclusion: We found that more than 50% of our patients on dialysis did not have pruritus. Moreover, there was insignificant relationship between dietary intake and pruritus. On the other hand, we discovered a substantial rise in the biochemical marker creatinine and pruritus, which was strongly present in our patients.

Keywords: Chronic kidney disease, creatinine, dialysis, diet, pruritus



1. INTRODUCTION

Pruritus is a relatively common and troubling symptom in patients with chronic kidney disease (CKD), specifically those who undergo renal dialysis. Different stimuli sensed by specialized cutaneous somatosensory nerve endings may cause itching, pain, and other sensations (Combs et al., 2015). The causes of pruritus in CKD patients may differ from those in other patients (Shirazian et al., 2017). The aberrations specific to uremia that have been found to trigger itch fibers include increased serum levels of calcium and phosphorus and influences of substances that start itching, such as substance P and histamine (Tinôco et al., 2018).

Skin abnormalities may link to structural alterations in the skin related to dehydration, increased systemic inflammation and immune dysregulation of uremia. Pruritus in patients undergoing dialysis may be related to three types of abnormalities: CKD and dialysis, abnormalities in the skin or associated with the regulation of itch sensation by the central nervous system. The preferred strategy for treating pruritus related to dialysis patients involves combining therapies to treat these triple etiologies (Shirazian et al., 2017; Tinôco et al., 2018).

Prior studies highlight the need to monitor the serum levels of mineral metabolism by laboratory tests, particularly serum levels of calcium and phosphorus among CKD patients undergoing renal dialysis (Peres et al., 2014; Tinôco et al., 2018). The KT/v is an important indicator of adequate renal dialysis treatment levels. The recommended value must be greater than 1.2 to indicate appropriate renal dialysis. It is calculated based on blood tests before and after renal dialysis (Kopple, 2001; Ashby at al., 2019). Another previous study concluded that 53.8% of patients undergoing renal dialysis have pruritus. In these patients, levels of potassium and phosphorus were elevated, which can point to a defect in the diet of patients undergoing renal dialysis (Kimata et al., 2014). In this context, it is essential to investigate possible associations of pruritus, such as non-adherence to a prescribed diet and changes in serum biochemical indicators of kidney function. However, the presentation of pruritus in CKD can be variable, which makes it difficult to differentiate it from other causes of itching. Consequently, this research aims to ascertain pruritus' prevalence and assess its relation to dietary intake and laboratory findings among renal dialysis patients in KAUH, Jeddah, Saudi Arabia.

2. MATERIAL AND METHODS

This study was conducted at the dialysis center in King Abdulaziz University Hospital (KAUH), a tertiary center in Jeddah, Saudi Arabia, from January to November 2022. It is conducted by the department of medicine and approved by the Research Ethics Committee at KAUH. Forty-four patients in the dialysis center were interviewed and studied during dialysis. Adult patients on hemodialysis were included and patients younger than 18 were excluded.

First, the following variables were assessed via an interview survey: Gender, age, marital status, occupation (active, retired or unemployed), presence of pruritus (yes or no), validated numerical rating scale of pruritus (from 0 to 10) (Phan et al., 2012; Reich et al., 2016; Reich et al., 2017; Verweyen et al., 2019; Storck et al., 2021), the number of renal dialysis per week, duration of dialysis (months), estimation of water intake, a 24 h recall for total protein and phosphorus intake and a food frequency questionnaire for estimation of sodium, phosphorus and potassium intake. After that, the medical records were reviewed for the last routine monthly blood work for laboratory data, including pre-dialysis urea, post-dialysis urea, creatinine, potassium, calcium and phosphate. Lastly, the patient file was reviewed for pre-dialysis weight, post-dialysis weight and adequacy of dialysis (KT/v).

The 24 hours recall was divided into three groups: Meat and egg, dairy products and legumes. Every serving in the meat and egg group contained 7 g of protein and 68 mg of phosphorus. Also, every dairy product group serving contained 4 g of protein and 110 mg of phosphorus. In the legumes group, every serving had 7 g of protein; the phosphorus was 180 mg in lentils, 135 mg in chickpeas and 125 mg in beans. The maximum amount of protein is 1 g/kg/day, for phosphorus, it is 1200 mg/day and for water, intake is 750 ml/day.

On the other hand, in the food frequency questionnaire, the reported frequency in a day was as reported. The reported frequency information was converted to daily frequency as follows: Reported frequency in a month divided by 30 (e.g., one time per month converted to 0.033 per day) and the reported frequency in a week divided by 7. The maximum frequency was two times per day for sodium and potassium. However, for the phosphorus group, the maximum frequency was one time/week (0.143/day), except for dairy products was one time/day.

Regarding the laboratory data, the range in the KAUH system is as follows: Urea (3.2-8.2 mmol/L), creatinine (61.9 to 114.9 μ mol/L) for men and (53 to 97.2 μ mol/L) for women, potassium (3.5-5.1 mmol/L) calcium (2.08-2.65 mmol/L) and phosphate (0.78-1.65 mmol/L). In accordance with the National Kidney Foundation Disease Outcomes Quality Initiative, the KT/v must be greater than 1.2 to indicate adequate dialysis (Stolic et al., 2010).

Fluid retention was calculated using the following formula: If the weight difference (pre-dialysis weight minus post-dialysis weight) was more than 4% of the post-dialysis weight (dry weight), it means fluid retention is present.

Statistical package for the social sciences version 21 was used for statistical analysis. The mean and standard deviation were calculated to describe continuous variables, while numbers and percentages were used for categorical variables. The student t-test and chi-square test were used to evaluate the differences between continuous and categorical variables. A p-value <0.05 was considered significant.

3. RESULTS

The participants enrolled in the study, as in Table 1, had an average age of 47 years; males comprised 18 (40.9%) and females 26 (59.1%) of the study population, 19 (43.2%) were single and 25 (56.8%) were married, 61% were unemployed, 22.7% were active, and 15.9% were retired. Pruritus was present in 40.9% of the participants, with an average scale of 4.9/10. Concerning adherence to the diet prescribed: For protein, 79.5% had suitable and 20.5% excessive; for phosphorus, 95.5% had appropriate and 4.5% excessive; for sodium, 65.9% had suitable and 34.1% excessive; for potassium, 43.2% had suitable and 56.8% had excessive; for water 47.7% had suitable and 52.3% had excessive intake. Fluid retention was present in 47.7% of the participants.

Before dialysis, eight of 20 subjects (40%) complained of pruritis; after dialysis, this had improved in three and remained unchanged in two. Two subjects who did not itch pre-dialysis complained of itching post-dialysis. Regarding Table 3, pruritus was present in 100% of patients with an excessive phosphorus diet; on the other hand, it was absent in 61% of patients following a controlled diet (p-value=0.162). In addition, pruritus was absent in patients following either controlled or excessive protein diets (54.3% and 77.8%, respectively) (p-value=0.270). Regarding sodium diet, pruritus was absent in patients with excessive intake (86.7%) and present in (55.2%) of patients following a controlled sodium diet (p-value=0.019). Apart from this, pruritus was absent in patients who had normal potassium levels (67.7%) and was higher in patients who had elevated potassium levels (61.5%) (p-value=0.143). Concerning K/tv, pruritus was absent in patients with appropriate K/tv levels (64.9%). In contrast, it was present in (71.4%) of patients with inappropriate K/tv levels.

Tables 1 and 3 exhibit the biochemical indicators of kidney function, which were analyzed quantitatively. 100% of the participant had high pre-dialysis urea, 11.4% had high post-dialysis urea, 36.4% had high phosphorus levels, 29.5% had elevated potassium levels, 6.8% had high albumin and 84.1% had appropriate KT/v.

Table 1 Socio-demographic and clinical characterization of chronic kidney patients undergoing hemodialysis Jeddah, KAUH, 2022

Variables	n = 44		
Gender			
Male	18 (40.9%)		
Female	26 (59.1%)		
Age, years	47*±17.5		
Marital status			
Single	19 (43.2%)		
Married	25 (56.8%)		
Occupation			
Unemployed	27 (61.4%)		
Active	10 (22.7%)		
Retired	7 (15.9%)		
Pruritus			
Present	18 (40.9%)		
Absen	26 (59.1%)		
Water intake			
Suitable	21 (47.7%)		
Excessive	23 (52.3%)		
Phosphorus intake			
Suitable	42 (95.5%)		
Excessive	2 (4.5%)		

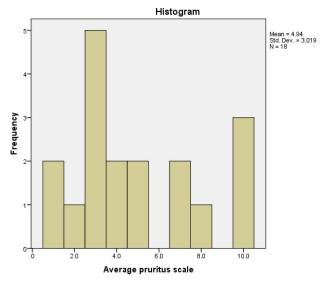
Protein intake			
Suitable	35 (79.5%)		
Excessive	9 (20.5%)		
Sodium intake			
Suitable	29 (65.9%)		
Excessive 15 (34.1%)			
Potassium intake			
Suitable	19 (43.2%)		
Excessive	25 (56.8%)		
Fluid retention			
Yes	21 (47.7%)		
No	20 (45.5%)		
Ktv _ adequacy			
Appropriate	37 (84.1%)		
Not appropriate	7 (15.9%)		

Variables expressed in n (Numbers and percent);

Table 2 shows the average laboratory values analysis: Pre-urea (18.7 mmol/L); post-urea (5.705 mmol/L); albumin (40.6 g/L); pre-creatinine (769 μ mol/L); calcium (2.1 mmol/L); phosphorus (1.5 mmol/L); pre-potassium (4.8 mmol/L); and KT/v with an average of 1.6.

Table 2 Characterization of laboratory data of patients undergoing hemodialysis

Laboratory	Arronago	Standard	
data	Average	deviation	
Pre-Urea	18.7	4.6	
Post-Urea	5.705	2.3	
Creatinine	769	202.6	
Calcium	2.1	0.24	
Albumin	40.6	4.1	
Potassium	4.8	0.85	
Phosphorus	1.54	0.55	
KT/v	1.57	0.34	



Kolmogorov-Smirnov test

Graph 1 Average pruritus scale in chronic kidney patients undergoing hemodialysis Jeddah, KAUH, 2022

^{*}Mean ± standard deviation in descriptive statistics.

Table 3 presents the result of the relation between the presence and absence of pruritus with adherence to the prescribed diet, serum level of biochemical indicators of kidney function and the adequacy of dialysis. The results indicate no significant statistical association between pruritus and excessive dietary intake of protein, phosphorus, sodium and potassium.

Table 3 Statistical association between adherence to the prescribed diet, biochemical indicators of kidney function and the quality of dialysis to the presence or absence of pruritus in chronic kidney patients undergoing dialysis Jeddah, KAUH, 2022

	J 1	U	0)	
Eating habits/	Pruritus	Pruritus		
Laboratory tests	Present	Absent	P value	
Protein Intake				
Follow diet	45.7%	54.3%	0.270^{2}	
Excessive	22.2%	77.8%		
Phosphorus Intake				
Follow diet	38.1%	61.9%	0.162^{2}	
Excessive	100%	0%		
Sodium Intake				
Follow diet	55.2%	44.8%	0.019^{1}	
Excessive	13.3%	86.7%]	
Potassium Intake				
Follow diet	42.1%	57.9%	1.000^{1}	
Excessive	40%	60%	1	
Water intake				
Follow diet	50%	46.2%	1.000^{1}	
Excessive	50%	53.8%		
Pre-Urea				
Normal	0%	0%	1 -	
Elevated	40.9%	59.1%		
Post-Urea	•			
Normal	38.2%	61.8%	0.865^{2}	
Elevated	60%	40%]	
Calcium				
Normal	36.4%	63.6%	0.759^{1}	
Elevated	0%	0%	1	
Albumin				
Normal	41.2%	58.8%	0.706^{2}	
Elevated	66.7%	33.3%	1	
Potassium				
Normal	32.3%	67.7%	0.143^{1}	
Elevated	61.5%	38.5%	1	
Phosphorus				
Normal	40%	60%	0.394^{2}	
Elevated	50%	50%	1	
KT/v				
Appropriate	35.1%	64.9%	0.103^{2}	
Not Appropriate	71.4%	28.6%]	
¹Chi-square test, ²Fisher's exact te	oct	•	•	

¹Chi-square test, ²Fisher's exact test

The result in Table 4 indicates that the mean pre-creatinine in the presence of pruritus was significantly different from the mean pre-creatinine in the absence of pruritus (P = 0.005).

Table 4 Statistical association between the biochemical indicators of kidney function quantitatively and the occurrence of pruritus in chronic kidney patients undergoing dialysis Jeddah, KAUH, 2022

		Pre-Creatinine	Pre-Urea	Pre-Potassium	Phosphorus
Pruritus	P Value	0.005	0.088	0.070	0.089

T-test for equality of means

4. DISCUSSION

A typical symptom of chronic kidney disease is pruritus. Other studies note that cutaneous symptoms affect the quality of life, depressive symptoms and sleep disorders, increasing the risk of morbidity in these patients (Kimata et al., 2014). Therefore, we aimed to investigate pruritus prevalence in renal dialysis patients at KAUH, Jeddah, Saudi Arabia. Furthermore, we assessed the importance of evaluating and monitoring its association with dietary intake and laboratory findings.

The diet restrictions recommended for renal dialysis patients are difficult to follow and at the same time, they may result in nutritional deficiencies (Luis et al., 2016). Eating foods with high sodium should be avoided since the body's response to high-sodium food is thirst and these patients have restrictions on liquids (Rodrigues et al., 2015). The appropriate protein intake is less than 1.1 g/kg/day, given the need for and prevention of protein malnutrition (Naylor et al., 2013).

Patient hemodialysis and water and dietary intake restriction are necessary for providing proper treatment. However, not all patients can comply with these water and dietary restrictions. Moreover, combining hemodialysis with dietary restrictions and water is necessary to obtain the correct treatment. Nevertheless, many patients understand the relevance of such restrictions. Still, they do not always manage to fulfill them (Coutinho and Costa, 2015), which would require changing their habits and eliminating shared family preferences (David et al., 2013).

Studies have shown that just 31.4% of their patients followed dietary and water restrictions. 40.5% of patients followed partially, while 28.1% followed the diet restrictions (David et al., 2013). The reasons for the deficiency in the follow-up process include the necessity of being regularly connected to the dialysis machine, which discourages the integral care of water and food restrictions, making them feel careless about their own life. Our study showed that concerning adherence to the diet prescribed, a phosphorus intake of 95.5% was suitable and 4.5% was excessive; a protein intake of 79.5% was suitable intake and 20.5% was excessive, sodium intake of 65.9% was suitable and 34.1% were excessive. A potassium intake of 43.2% was suitable and 56.8% was excessive.

The accumulation of urea to a certain concentration in blood levels leads to toxic effects responsible for itching (Costa et al., 2015). The toxins and uremia disappear under hemodialysis treatment. This justifies the literature results concerning urea post-dialysis, in which 55 individuals regularized their urea levels and only 12 reported itching. However, 38.2% of our patients with normal post-urea levels complained of pruritus in this context.

KT/v is an indicator of the dose of dialysis offered to the patient with chronic kidney disease (CKD), showing the adequacy of dialysis; when you know the values of debugging the dialyzer (K), the volume of urea distributed in the patient to be removed (V) and the session time hemodialysis (T) (Guanaré et al., 2016). This study shows an insignificant relation between KT/V and pruritus. Furthermore, the KT/v adequacy rate was 84.1%. However, the lack of statistical correlation between the variables points to the efficacy of dialysis as a potential barrier to developing pruritus.

There was no statistically significant association between biochemical findings and pruritus, except for creatinine, with a p-value of 0.005 in the literature, a study showed the same results, finding no association between pruritus and biomedical indicators, except for serum calcium level (Tinôco et al., 2018). In comparison, another study emphasized an association between pruritus and high serum calcium and phosphorus (Kimata et al., 2014).

Furthermore, our study was limited to one center, which reflected our sample size and subjective communication with patients in recalling the exact amount of food intake. Moreover, there were missing weight measurements for three patients in our sample regarding fluid retention equations. However, we used a food frequency questionnaire and a 24-hour recall questionnaire on dietary intake. The previous will add strength in collecting the food intake habits over a month and converting this to a daily frequency.

5. CONCLUSION

This study found that more than half of the patients on dialysis did not have pruritus. Additionally, there was no significant relationship between dietary intake and symptoms of pruritus. In contrast, we discovered a positive relationship between increased creatinine levels of creatinine and the presence of pruritus in our patients. Adequate care and preventative measures as treatment strategies for CKD patients may reduce preventable hospitalizations. More researches with a larger sample size and documenting

daily food amounts for better recall to minimize possible mistakes can help us understand these relations better. This can be achieved by conducting a multicenter study, enabling future researchers to generalize their results to a broader region. Additionally, more studies will help confirm our proposed theories.

Ethical approval

The protocol of this study was completed to acclimate with the Declaration of Helsinki and was affirmed by the Research Ethical Committee of King Abdulaziz University. Approval number is (HA-02-J-008). Informed consent from all enrolled patients was obtained or their legal representatives.

Informed Consent Statement

Verbal informed consent has been obtained from each participant.

Funding

This study has not received any external funding.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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